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Dennis Rylatt

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EXAMINER

OLSEN, KAJ K

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/556,910	Applicant(s) RYLATT ET AL.	
	Examiner KAJ K. OLSEN	Art Unit 1724	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28,30 and 31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28,30 and 31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/18/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 2 and 3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

3. Claims 2 and 3 are drawn to the use of the claimed cell separation process for a number of specific types of cells. However, except for erythrocytes and leukocytes, applicant has not enabled one of ordinary skill in the art to extend the claimed process to any of the other identified cells of these claims. In particular, applicant only demonstrated the use of this process for separation of red and white blood cells and appeared to rely on the fact that these two types of cells have sufficient charge to induce useful electrophoretic movement and have different ranges of sizes allowing one to separate them from each other by size exclusion (specification p. 10, ll. 3 and 4). This would clearly not be universal phenomenon automatically applicable to other cell types and more than routine skill in the art would be necessary to extend this device to these other types of cells being explicitly claimed. Applicant has not demonstrated for any of these other types of cells that similar conditions can be established. One possessing ordinary skill in the art would not have been enabled to utilize the claimed invention for these other specific cells of claims 2 and 3.

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4. Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The examiner cannot find support for the limitation that the movement from the electric potential is substantially greater than any convective movement of the desired cell type. All the specification seemed to suggest is that the ion-permeable barriers substantially prevents convective movement, but the specification doesn't appear to have ever explicitly suggested that the electric potential movement was substantially greater than any convective movement.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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7. The examiner has withdrawn the previous rejection of the claims over the teaching of Egen with or without O'Farrell in view of the amendment to claim 1.

8. Claims 1-28, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prince et al (USP 6,491,819) in view of either CN 1048168A (hereafter "CN '168") or Armstrong (USP 7,214,299) and Vigh et al (US 2002/0043465). CN '168 and Armstrong are being cited and relied on for the first time with this office action. Their use here was necessitated by the applicant's amendment. For CN '168, the examiner is relying on the provided translation of the document.

9. With respect to claim 1, Prince discloses a method of separating a cell type from a mixture of cell types that comprises providing a first membrane 100 separating a first chamber from a second chamber (i.e. the upper and lower sides respectively of 100 in fig. 6 and 7) which allowed Prince to separate red blood cells from white blood cells. See col. 10, ll. 6-25. Prince further teaches that the flow parallel to the membranes with the addition of a perpendicular flow can be utilized to enhance the separation of the red blood cells from the white blood cells (col. 10, l. 25 – col. 11, l. 29). With respect to this membrane being ion permeable, a porous membrane would inherently be permeable to ion movement. Prince does not explicitly suggest the use of an electric field to induce that perpendicular cell flow. However, both CN '168 and Armstrong demonstrate that electrophoresis can be utilized as the sole means of inducing cell flow either through a membrane or through a porous media. In particular, CN '168 teaches that one type of sperm cell can be separated from another type of sperm cell via an electric potential that induces the cell flow through a semipermeable membrane 4. See p. 6, ll. 2-22. Armstrong teaches that cells, including blood cells, can be separated from each other via an induced electric

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field providing electrophoretic force to the cells through a porous polymer media. See col. 2, ll. 28-40; col. 7, ll. 13-53 and col. 9, ll. 43-45. It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teachings of CN '168 or Armstrong and rely on an electric field to generate a transverse force for Prince because the utility of one known means of inducing cellular movement for another means requires only routine skill in the art. With respect to the new limitation specifying that all transbarrier migration of the desired cell type occur upon application of the electric potential, both CN '168 and Armstrong are not applying any other means of force (such as a counter flow) to the cells to induce their movement, so all the force inducing the cells through the membranes of porous material is induced by the application of electric potential. With respect to the claimed arrangement of first and second electrolyte chambers with the second and third ion permeable barriers between the sample chambers and the electrolyte chambers, Vigh teaches a conventional electrophoretic device for generating perpendicular electrophoretic movement and explicitly teaches the use of second and third ion permeable barriers to separate the electrolyte chambers from the sample chambers presumably to keep the sample constituents from reaching either the electrolyte chambers or the electrodes and to keep the electrolyte from mixing with the sample. See par. 0080 and 0081. It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Vigh for the process of Prince in view of CN '168 or Armstrong so as to keep the sample constituents within the sample chambers and the electrolyte within the electrolyte chambers.

10. With respect to claim 2-4, Prince is separating erythrocytes from leukocytes, which are two cell populations.

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11. With respect to claim 5, red blood cells are presumably a wanted type of cell that is passed through the ion barrier.

12. With respect to claim 6, CN '168 and Armstrong rely on the electrophoretic force for the transbarrier migration.

13. With respect to claim 7, this is an inherent function of the use of ion permeable barriers. In particular, Prince is relying on a first ion permeable barrier serving analogous function to the first permeable barrier of the present invention (i.e. allow red blood cells to transmigrate but not white blood cells) and the second and third ion permeable barriers of Vigh.

14. With respect to claim 8, it clearly would have been obvious to one of ordinary skill in the art to apply the potential long enough to generate the desired level of purity of sample.

15. With respect to claims 9-11 and 14-17, see Prince col. 7, ll. 34-39 and Vigh par. 0080 and 0081.

16. With respect to claims 12 and 13, see Prince col. 7, ll. 10-25.

17. With respect to claims 18 and 19, both CN '168 and Armstrong stressed that the electrophoresis must be done under conditions that maintain the vitality of the cells being separated. See CN '168 p. 5, ll. 1-5 and Armstrong col. 7, ll. 13-22. One of the ordinary skill in the art would recognize that electrophoretic voltages and solution choices should be tailored to maintain greater than 50% or 60% viability of the cells after separation.

18. With respect to claim 20, both batch and continuous measurements are obvious choices of separation schemes.

19. With respect to claims 21-24, finding the necessary field strength to induce the desired separation of the cells without lysing or rupturing the cells requires only routine skill in the art.

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20. With respect to claims 25 and 26, finding the amount of time necessary to arrive at the desired level of cell separation, including the use of 1-60 minutes or 10 minutes, would have required only routine skill in the art.

21. With respect to claim 27, both CN '168 and Armstrong teach the use of buffered solutions for the cell samples. See CN '168 p. 6, ll. 1 and 2 and Armstrong col. 7, ll. 13-22. Finding the appropriate buffer concentration that provides an effective electrophoretic medium while keeping the cells viable, including the use of 100-400 mM of concentration, requires only routine skill in the art.

22. With respect to claim 28, see Armstrong col. 11, ll. 20-27. The examiner believes the disclosed tris solution is the same thing as Bis Tris.

23. With respect to claim 30, finding the concentration of cell mixture that can be effectively utilized with the device, including the use of 10^6 to 10^8 cells/mL, requires only routine skill in the art.

24. With respect to claim 31, Prince discloses a first ion-permeable barrier substantially analogous in function to first ion-permeable barrier of the present invention (see the discussion above), and the present invention specification evidences that it is the ion-permeable barrier that is preventing the convective mixing of the cells (p. 4, ll. 24-29). Hence, the barrier of Prince would inherently prevent convective mixing and presumably the electrophoretic movement suggested by CN '168 and Armstrong would be substantially greater than any convective movement of the cells.

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25. Claim 28 in the alternative is rejected under 35 U.S.C. 103(a) as being unpatentable over Prince in view of either CN '168 or Armstrong and Vigh as applied to claim 27 above, and further in view of Egen et al (USP 5,336,387).

26. In the rejection of claim 28, the examiner believes the Tris solution disclosed by Armstrong is the same thing as Bis Tris. However, even if the examiner is incorrect, Egen already disclosed that glucose and sucrose can be utilized as a buffer for the electrophoresis of blood cells. See col. 16, ll. 39-41. It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Egen for the method of Prince and CN '168 or Armstrong and Vigh because the substitution of one known buffer for another requires only routine skill in the art.

Response to Arguments

27. Applicant's arguments filed 10/18/2010 have been fully considered but they are either not persuasive or are moot in view of the new grounds of rejection necessitated by the applicant's amendment. With respect to the 112 rejection of claims 2 and 3, applicant urges that the examiner is misreading the elements of claims 2 and 3 in that the cell types need not be from the same cell type. The examiner does not understand this argument as the examiner never alleged said the cells have to be of the same type. In fact, the examiner discussed how the working example was enabling for separating erythrocytes from leukocytes (i.e. two different cell types). Moreover, the applicant appears to have missed the point of this rejection. In claims 2 and 3, applicant has set forth specific types of cells that the applicant has not set forth any guidance as to how the technique of the present invention could be applicable to any of the specific types of

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cells discussed. For example, are any of these other specifically listed cells even viable for electric field induced transbarrier migration? Electrophoresis of cells is notoriously difficult because most cells have a large mass (and consequently a very mass to charge ratio), which makes it very difficult to move the cells under an electric field. Almost all of the cited art for the electrophoretic movement of cells cited both here and in the previous office action are drawn to the movement of erythrocytes and leukocytes, which is the only specific embodiment of the present invention. Hence the applicant's working example is limited to one of the few cell types extensively demonstrated as being viable with electrophoresis. Most cells, including a number of the specific cell classes listed in claims 2 and 3 are considerably larger than the erythrocytes of the present invention, which would render electrophoresis considerably more difficult, if not impossible. Moreover, Coster (USP 4,055,799) demonstrates that many cells will rupture in the presence of an electric field comparable to the electric fields of the present invention and of the prior art electrophoresis. Hence in the absence of any guidance in the specification as to how the technique of the present invention can be extended to these other specific cell classes, applicant is not enabled for claiming these specific cell classes.

28. Applicant also urges that they also disclose separating cell populations based on charge. However, considering that the applicant has no working examples demonstrating the viability of charge being the way the cell types are differentiated from each other, the examiner does not believe applicant would be enabled for the use of charge as being the differentiating mechanism.

29. With respect to the previous art rejection, applicant urges that the various secondary teachings of Egen, Sammon or Ivory in the rejection relying on Prince as a primary teaching do not demonstrate that substantially all the transbarrier migration occurs with the electric potential.

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Without conceding whether or not these various secondary teachings would render obvious the use of the transmembrane migration being substantially from the application of electric potential, the examiner has introduced the teachings of CN '168 and Armstrong that rely on electric fields alone to provide the separation of cells. Applicant's remaining arguments are moot in view of these new teachings.

Conclusion

30. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAJ K. OLSEN whose telephone number is (571)272-1344. The examiner can normally be reached on M-F 6:00-2:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam X. Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kaj K Olsen/
Primary Examiner, Art Unit 1724

December 18, 2010